REMARKS

Claims 27-39 are pending in the present application and at issue. Claim 35 has been amended to incorporate the subject matter of claim 37. Claim 36 has been rewritten as an independent claim. Claim 37 has been amended to depend from claim 36.

It is respectfully submitted that the present amendment presents no new issues or new matter and places this case in condition for allowance. Reconsideration of the application in view of the above amendments and the following remarks is requested.

I. The Rejection of Claims 27-35 and 38-39 under 35 U.S.C. 112

Claims 27-35 and 38-39 are rejected under 35 U.S.C. 112, as failing to comply with the written description requirement. Specifically, the Office stated that the phrases "identity of at least 90% in claim 27 and "identity of at least 95%" in claim 32 cannot be found in any of the parent applications." This rejection is respectfully traversed.

Claims 27 and 32 are directed to methods for improving the nutritional value of an animal feed, comprising adding to the animal feed an acid-stable protease that comprises an amino acid sequence having an identity of at least 90% or 95%, respectively, to SEQ ID NO: 1.

Proteases having an amino acid sequence having an identity of at least 90% or 95% to SEQ ID NO: 1 are supported by page 4, lines 3-9 of the instant application and page 4, lines 24-34 of the parent application (U.S. Application No. 09/779,323).

Since the phrases are fully supported by the instant and parent applications, the claims comply with the written description requirement.

For the foregoing reasons, Applicants submit that the claims overcome this rejection under 35 U.S.C. 112. Applicants respectfully request reconsideration and withdrawal of the rejection.

II. The Rejection of Claim 35 and 38-39 under 35 U.S.C. 112

Claims 35 and 38-39 are rejected under 35 U.S.C. 112, as failing to comply with the written description requirement. Specifically, the Office stated that "currently it is unknown how much structural homology or identity exists among the genus of proteases from Nocardiopsis protease origin."

Claim 35 has been amended to incorporate the subject matter of claim 37. Applicants therefore submit that this rejection has been overcome.

III. **The Rejection of Claims 27-35 and 38-39 under 35 U.S.C. 102**

Claims 27-35 and 38-39 are rejected under 35 U.S.C. 102(b) as anticipated by Oestergaard et al. (WO 01/58276). Specifically, the Office states that "the examiner could not find support for '90% identity' or '95% identity' in any of the parent applications. Therefore, the earliest filing date that instant claims benefit from is 11/14/2003." This rejection is respectfully traversed.

This application is a continuation of U.S. Application No. 09/779,323 filed February 8, 2001. As discussed above, the parent application fully supports the phrases "90% identity" or "95% identity" at page 4, lines 24-34. Applicants therefore submit that Oestergaard et al. is not prior art.

For the foregoing reasons, Applicants submit that the claims overcome this rejection under 35 U.S.C. 102. Applicants respectfully request reconsideration and withdrawal of the rejection.

IV. **The Rejection of Claims 27-35 and 38-39 under 35 U.S.C. 103**

The Office maintained the rejection of claims 27-35 and 38-39 under 35 U.S.C. 103 as being unpatentable in view of Bedford et al. (WO 96/05739) in view of Snow-Brand-Milk-Prod. (JP 02255081). This rejection is respectfully traversed.

Snow-Brand-Milk-Prod. discloses a *Nocardiopsis* protease. However, Snow-Brand-Milk-Prod. does not teach or suggest the use of proteases in animal feed.

Bedford et al. disclose an enzyme feed additive comprising a xylanase, a protease and optionally a beta-glucanase, wherein the ratio between the xylanase and beta-glucanase activities lies within a certain specified range. At page 25, lines 2-5, Bedford et al. disclose that the protease is a subtilisin which can be derived from the genus *Bacillus*. Bedford et al. further disclose that the protease may be one of the following commercially available proteases: NEUTRASE™, PURAFECT™, SAVINASE™, MAXACAL™, DURAZYM™ and MAXAPEM™, or a mutant subtilisin described in one of a number of published patent applications. None of the proteases disclosed in Bedford et al. are acid-stable.

The feed additives described in Bedford et al. are said to have an improved (i.e., lower) feed conversion ratio (FCR), which results in more efficient utilization of the feed. However, the results shown in Bedford et al. do not prove Bedford et al.'s allegations of improved FCR.

The only experiments using a protease described in Bedford et al. are provided in Examples 2 and 5. However, as explained in the prior response, the results disclosed in the examples do not suggest to one of ordinary skill in the art that there is an improvement in FCR by using a protease in an animal feed.

In the experiment described in Example 2, chickens were treated with a control animal feed (with no enzymes), an animal feed designated "Z", which is identical to the control except that it also contains xylanase, three animal feeds designated "A," "C," and "E", which are identical to Z except that they contain the protease NEUTRASE™, and three animal feeds designated "B," "D" and "F", which are also identical to Z except that they contain a modified *Bacillus amyloliquefaciens* subtilisin.

The results, which are provided in Table 4, show that the use of the control animal feed and the animal feed designated Z resulted in an FCR of 1.85, the use of the animal feeds designated A, C and E resulted in an FCR of 1.85, 1.85 and 1.82 (i.e., two of the animal feeds containing the protease NEUTRASE™ resulted in the same FCR as the control animal feed and the animal feed designated Z), and the use of the animal feeds designated B, D and F resulted in an FCR of 1.82, which is only a fraction below the FCR obtained with the control animal feed and the animal feed designated Z. The results do not demonstrate that there is any statistical significant difference between the results obtained using the control animal feed and the animal feed designated Z, on the one hand, and the results obtained using the animal feeds designated A-F, on the other hand. Thus, the results of Example 2 would not suggest to one of ordinary skill in the art that there is an improvement in FCR by using a protease in an animal feed.

Similarly, the results in Example 5 shown in Table 9, do not demonstrate that there is any statistical difference between using a protease-free animal feed and a protease-containing animal feed. Thus, the results of Example 5 also would not suggest to one of ordinary skill in the art that there is an improvement in FCR by using a protease in an animal feed.

That the results in Bedford et al. do not show an improvement in FCR by using a protease is confirmed in the Declaration under 37 C.F.R. 1.132 of Carsten Sjøholm, which was filed during prosecution of the parent application and submitted with the prior response. Mr. Sjøholm explains that the results disclosed in Bedford et al. do not prove to one of ordinary skill in the art that the addition of a protease to an animal feed results in an improved feed conversion ratio.

Applicants also previously submitted a copy of a Declaration under 37 C.F.R. 1.132 of Anna-Maria Klünter, which was also filed during prosecution of the parent application. The Klünter declaration describes a set of experiments in which chickens were fed feed compositions with or without the *Nocardiopsis* protease of SEQ ID NO: 1. Dr. Klünter reports that the results of the experiments "clearly demonstrate that broiler chickens have a significantly improved weight gain and significantly improved feed conversion when fed an animal feed composition comprising the *Nocardiopsis* protease." Dr. Klünter also concludes that the results are surprising and unexpected.

These results demonstrate that broiler chickens have a significantly improved weight gain and significantly improved feed conversion when fed an animal feed composition comprising an acid-stable protease. The acid-stable proteases recited in the claims differ significantly in structure (low identity) and function (acid stability) from the proteases of Bedford et al. Based on the general knowledge in the art and in particular, Bedford et al., an artisan would not expect that all proteases are suitable for use in feed let alone that the acid-stable proteases recited in the claims of the present invention would be useful for improving the nutritional value of feed.

Notwithstanding Applicants' showing of surprising and unexpected results, the Office sated that Applicants' arguments were unpersuasive.

First, the Office states that "even if one focused on results obtained by Bedford et al., the fact ... that Bedford et al. do not display a significant improvement of FCR in the presence of its alkaline protease only motivates one of ordinary skill to try incorporate new proteases (such as acid stable protease of Snow-Brand)...." This is respectfully traversed.

Because the results disclosed in Bedford et al. are on their face unconvincing, persons of ordinary skill art would not be motivated to incorporate other proteases. The results in Bedford et al. do not show that there is any advantage to using a protease in animal feed. Even if they were motivated to incorporate other proteases, they would use proteases having similar properties and similar sources as the proteases disclosed in Bedford et al., such as alkaline *Bacillus* proteases. There is no suggestion in Bedford et al. to use an acid-stable protease, *e.g.*, from *Nocardiopsis*.

Second, the Office states that "protein solubility, whether surprisingly and unexpectedly improved or not, in isolation, cannot be automatically translated into improvement of nutritional value of animal feed. This is also respectfully traversed.

Applicants do not rely solely on protein solubility data to show that the protease of SEQ ID NO: 1 improves the nutritional value of animal feed. In the declaration of Anna-Maria Klünter, Applicants submitted *in vivo* results demonstrating that broiler chickens have a significantly improved weight gain and significantly improved feed conversion when fed an animal feed composition comprising the protease of SEQ ID NO: 1 compared with the same animal feed composition without protease.

Third, the Office states that "(a) said data has only been compared to a chicken feed completely lacking protease and not with a feed that comprises alkaline protease of Bedford.... (b) The displayed improvements in Klunter's declaration are hardly significant and unexpected and appear to only demonstrate a minor improvement over feed with no protease. (c) Klunter's data

again appears to only refer to utilization of SEQ ID NO: 1 and not its claimed homologs." This is respectfully traversed.

It is unnecessary to compare the protease of SEQ ID NO: 1 and Bedford et al.'s alkaline proteases because Bedford et al. have already demonstrated that they have no effect. Furthermore, the Klunter Declaration includes a statistical analysis of the results and demonstrates that broiler chickens have a significantly improved weight gain and significantly improved feed conversion when fed an animal feed composition comprising the protease of SEQ ID NO: 1. Finally, the proteases recited in Applicants' claims are structurally similar to the protease of SEQ ID NO: 1 (90-95% identical) and therefore would be expected to have properties similar to the protease of SEQ ID NO: 1.

For the foregoing reasons, Applicants submit that the claims overcome this rejection under 35 U.S.C. 103. Applicants respectfully request reconsideration and withdrawal of the rejection.

V. Conclusion

In view of the above, it is respectfully submitted that all claims are in condition for allowance. Early action to that end is respectfully requested. The Examiner is hereby invited to contact the undersigned by telephone if there are any questions concerning this amendment or application.

Respectfully submitted,

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